

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-33 (Cancel).

34. (New) A herpes simplex virus (HSV) comprising:
- (i) an HSV LAT sequence inserted into:
 - a gene of said HSV which is essential for the replication of said HSV;
or
 - a gene region spanning the site of said gene,wherein said HSV LAT sequence is an HSV1 or HSV2 sequence which:
 - corresponds to all or part of the sequence of HSV1 strain 17 + defined by nucleotides 5,490 to 9,214 or 117,159 to 120,882; and
 - itself or together with a linked promoter drives long term expression of a heterologous gene operably linked thereto in a cell infected with said HSV; and
 - (ii) a deletion of the endogenous LAT sequences corresponding to those inserted into said gene or gene region.
35. (New) The virus according to claim 34 wherein the said gene essential for replication of said HSV is an immediate early (IE) gene selected from the group consisting of ICP27 and ICP4.
36. (New) The virus according to claim 34 wherein the deletion comprises at least 50% of the sequences present in the inserted LAT sequence.

37. (New) The virus according to claim 34 wherein the deletion comprises at least 75% of the sequences present in the inserted LAT sequence.
38. (New) The virus according to claim 34 wherein the deletion comprises at least all of the sequences present in the inserted LAT sequence.
39. (New) The virus according to claim 34 wherein the LAT sequence consists essentially of nucleotides 118866 to 120219 (SEQ ID NO:1) and/or nucleotides 117159 to 118865 (SEQ ID NO:2) of HSV1 strain 17+ (GenBank HE1CG), or the corresponding sequences of another HSV strain.
40. (New) The virus according to claim 34 wherein the said gene essential for replication of said HSV comprises a deletion that prevents replication.
41. (New) The virus according to claim 34 which is selected from the group consisting of an HSV1 strain, an HSV2 strain and an inter-type recombinant containing DNA from an HSV1 strain and an HSV2 strain.
42. (New) The virus according to claim 41 which is an HSV1 strain.
43. (New) The virus according to claim 34 which carries at least one heterologous gene.
44. (New) The virus according to claim 43 wherein said heterologous gene is operably linked to said inserted HSV LAT sequence.

45. (New) The virus according to claim 43 wherein said heterologous gene is operably linked to a control sequence permitting expression of said heterologous gene in mammalian cells.
46. (New) The virus according to claim 45 wherein said mammalian cell is a cell of the central or peripheral nervous system of a mammal.
47. (New) The virus according to claim 45 wherein said mammalian cell is a cell of the eye, heart or skeletal muscle of a mammal.
48. (New) The virus according to claim 43 wherein said heterologous gene encodes a polypeptide of therapeutic use.
49. (New) The virus according to claim 48 wherein said gene encodes a polypeptide which is cytotoxic.
50. (New) The virus according to claim 48 wherein said gene encodes a polypeptide capable of converting a precursor prodrug into a cytotoxic compound.
51. (New) The virus according to claim 43 wherein the heterologous gene is selected from the group consisting of genes encoding proteins involved in the regulation of cell division, genes encoding enzymes involved in metabolic pathways, genes encoding transcription factors and genes encoding heat shock proteins.
52. (New) A method for studying the function of a heterologous gene in a mammalian cell which method comprises:
- (a) introducing said heterologous gene into a herpes simplex virus comprising:
 - (i) an HSV LAT sequence inserted into:

- a gene of said HSV which is essential for the replication of said HSV;
or
- a gene region spanning the site of said gene,

wherein said HSV LAT sequence is an HSV1 or HSV2 sequence which:

- corresponds to all or part of the sequence of HSV1 strain 17 + defined by nucleotides 5,490 to 9,214 or 117,159 to 120,882; and
- itself or together with a linked promoter drives long term expression of a heterologous gene operably linked thereto in a cell infected with said HSV; and

(ii) a deletion of the endogenous LAT sequences corresponding to those inserted into said gene or gene region;

(b) introducing the resulting herpes simplex virus into said mammalian cell;

and

(c) determining the effect of expression of said heterologous gene in said mammalian cell.

53. (New) The method according to claim 52 wherein said heterologous gene is a wild-type or mutant gene implicated in causing disease.

54. (New) The method according to claim 52 wherein said mammalian cell is dysfunctional, said heterologous gene is wild-type and the effect of expression of said heterologous gene is determined by an assay for cellular function.

55. (New) The method according to claim 52 wherein said mammalian cell has one or more endogenous genes inactivated by mutation.

56. (New) A method for producing a herpes simplex virus comprising:

(i) an HSV LAT sequence inserted into:

- a gene of said HSV which is essential for the replication of said HSV;
or
- a gene region spanning the site of said gene,

wherein said HSV LAT sequence is an HSV1 or HSV2 sequence which:

- corresponds to all or part of the sequence of HSV1 strain 17 + defined by nucleotides 5,490 to 9,214 or 117,159 to 120,882; and
- itself or together with a linked promoter drives long term expression of a heterologous gene operably linked thereto in a cell infected with said HSV; and

(ii) a deletion of the endogenous LAT sequences corresponding to those inserted into said gene or gene region,

said method comprising:

- (a) inserting the HSV LAT sequence into an essential IE gene of the virus: and
- (b) deleting the endogenous LAT sequences in the virus.

57. (New) A composition comprising a carrier or diluent and a herpes simplex virus comprising:

- (i) an HSV LAT sequence inserted into:
 - a gene of said HSV which is essential for the replication of said HSV;
or
 - a gene region spanning the site of said gene,

wherein said HSV LAT sequence is an HSV1 or HSV2 sequence which:

- corresponds to all or part of the sequence of HSV1 strain 17 + defined by nucleotides 5,490 to 9,214 or 117,159 to 120,882; and
- itself or together with a linked promoter drives long term expression of a heterologous gene operably linked thereto in a cell infected with said HSV; and

- (ii) a deletion of the endogenous LAT sequences corresponding to those inserted into said gene or gene region;
and
- (iii) at least one heterologous gene.

58. (New) The composition according to claim 57 wherein the said gene essential for replication of said HSV is an immediately early IE gene selected from the group consisting of 1CP27 and ICP4.

59. (New) The composition according to claim 57 wherein the deletion comprises at least 50% of the sequences present in the inserted LAT sequence.

60. (New) The composition according to claim 57 wherein the deletion comprises at least 75% of the sequences present in the inserted LAT sequence.

61. (New) The composition according to claim 57 wherein the deletion comprises at least all of the sequences present in the inserted LAT sequence.

62. (New) The composition according to claim 57 wherein the LAT sequence consists essentially of nucleotides 118866 to 120219 (SEQ ID NO:1) and/or nucleotides 117159 to 118865 (SEQ ID NO:2) of HSVI strain 17+ (GenBank HE1CG), or the corresponding sequences of another HSV strain.

63. (New) The composition according to claim 57 wherein the said gene essential for replication of said HSV comprises a deletion that prevents replication.

64. (New) The composition according to claim 57 wherein said herpes simplex virus is selected from the group consisting of an HSV 1 strain, an HSV2 strain and an inter-type recombinant containing DNA from an HSV1 strain and an HSV2 strain.
65. (New) The composition according to claim 64 which is an HSV1 strain.
66. (New) The composition according to claim 57 wherein said heterologous gene is operably linked to said inserted HSV LAT sequence.
67. (New) The composition according to claim 57 wherein said heterologous gene is operably linked to a control sequence permitting expression of said heterologous gene in mammalian cells.
68. (New) The composition according to claim 57 wherein said mammalian cell is a cell of the central or peripheral nervous system of a mammal.
69. (New) The composition according to claim 57 wherein said mammalian cell is a cell of the eye, heart or skeletal muscle of a mammal.
70. (New) The composition according to claim 57 wherein said heterologous gene encodes a polypeptide of therapeutic use.
71. (New) The composition according to claim 57 wherein said gene encodes a polypeptide which is cytotoxic.
72. (New) The composition according to claim 57 wherein said gene encodes a polypeptide capable of converting a precursor prodrug into a cytotoxic compound.

73. (New) The composition according to claim 57 wherein the heterologous gene is selected from the group consisting of genes encoding proteins involved in the regulation of cell division, genes encoding enzymes involved in metabolic pathways, genes encoding transcription factors and genes encoding heat shock proteins.